UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,107	05/23/2005	Charlotta Olsson	1501-1276	5068

466 7590 12/10/2007

YOUNG & THOMPSON
745 SOUTH 23RD STREET
2ND FLOOR
ARLINGTON, VA 22202

EXAMINER
CROW, ROBERT THOMAS

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
12/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,107	OLSSON ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 9 October 2007 in which the specification and claims 1-6 and 8-16 were amended, claims 7 and 17-18 were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The objections to the specification listed not reiterated below are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

In view of Applicant's request on page 14 of the Remarks that the request for a terminal disclaimer be held in abeyance, the previous rejections under the judicially created doctrine of obviousness-type double patenting over claims 33-34 of copending Application No. 10/529,352 are **maintained** for the reasons set forth in the previous Office Action.

Claims 1-6 and 8-16 are under prosecution.

Specification/Noncompliant Amendment

2. Applicant's amendment to the Title is acknowledged and has been entered.

3. The disclosure is objected to because of the following informalities: as stated in the previous Office Action, the Preliminary Amendment filed 23 May 2005 changed the paragraph beginning with "Example 4" on page 30 of the specification with a paragraph reciting "Example 5," and also changed the paragraph beginning with "Example 5" on page 32 of the Specification with a paragraph reciting "Example 6." Thus, as a result of the amendment, there is no "Example 4" in the specification. It is

suggested the specification be amended to recite "Example 4" on page 30 and "Example 5" on page 32, so that the five examples presented are numbered sequentially.

4. It is emphasized that Applicant's response filed 9 October 2007 has been considered in the interest of customer service and compact prosecution. However, for the response to this Office Action to be complete, Applicant is **REQUIRED** to correct the errors listed above and file amendments that are compliant with 37 CFR 1.121. Failure to comply with this requirement will be considered **nonresponsive**.

Claim Objections

5. Claims 5 and 16 are objected to because of the following informalities:

Claim 5 recites "or b)" in the penultimate line of the claim; however, the recitation of "a)" has been deleted from the claim. Thus, "or b)" is not necessary.

Claim 16 recites each of the following, which appear to be typographical errors:

A. The recitation "The method claim 1" in line 1.

B. The recitation "selected form" in line 2.

C. The recitation "Triton X-100 proteins" in line 7.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 and 8-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. **This is a new matter rejection**. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1, upon which claims 2-6 and 8-16 depend, is amended to recite "and thereafter neutralizing the label by adding a label-interacting agent or by bleaching" as part of step d), which is followed by repeating steps c) to d) at least once. Thus, claim 1 now encompasses an embodiment wherein neutralization after each determination of the nucleotide added. Applicant cites claim 7 (now cancelled) as support for the amendment.

However, original claim 7 specifically recited a method "according to any one of claims 1-3, in which the label is neutralized **after** step d)" (emphasis added by examiner). In addition, both pages 4-5 of the specification teach "the label is neutralized **after** step d)" (emphasis added by examiner). Thus, the specification and original claim 7 only teach neutralization **after** step d), rather than **as part** of step d). The present amendment to claim 1 therefore encompasses at least one embodiment, wherein neutralization is performed after each round of determination of the type of nucleotide added to the primer, which is not supported by the specification. The addition of the neutralization step as part of step d) therefore constitutes new matter.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-6, 8-13, 13, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawashima et al (PCT International Application No. WO 98/44152, published 8 October 1998) in view of Urdea et al (U.S. Patent No. 4,910,300, issued 20 March 1990).

Regarding claims 1, 10, and 13, Kawashima et al teach a method for determining the sequence of a nucleic acid. In a single exemplary embodiment, Kawashima et al teach providing a single stranded form of a nucleic acid; i.e., a single stranded target nucleic acid (page 5, lines 15-20). The single stranded nucleic acid molecule is then hybridized to a primer to form a template/primer complex (page 5, lines 15-20). The primer is enzymatically extended by addition of a polymerase and extension with at least one nucleotide (page 6, lines 1-5) wherein the at least one nucleotide is a mixture comprising less than 50% of a labeled form of the at least one nucleotide (page 16, lines 15-23). The extension product comprising the labeled nucleotide is then detected (page 6, lines 6-10); because a given (i.e., single) nucleotide is provided in the extension step (page 6, lines 1-5), the type of nucleotide incorporated is known. The label is neutralized after the detection step by photobleaching; namely, laser bleaching of the fluorophores, which are labels (page 18, lines 13-19). Because labels are periodically photobleached after several extension and detection steps (page 18, lines 13-19 and page 6, lines 23-27), the removal occurs more than once (i.e., "periodically;" page 6, lines 23-27) after at least two repetitions of the detection step. Kawashima et al also teach the extension and detection steps are repeated at least once (page 6, lines 10-15).

It is noted that the open claim language "comprising" in line 2 of the claim encompasses additional steps between step d) and the "repeating steps c) to d) at least once" at the end of the claim. Thus, after a label is removed by photobleaching (i.e., step "d)" of the instant claims), multiple rounds of

enzymatic extension with a mixture of labeled and unlabeled nucleotides and determination of the type of nucleotide added before a subsequent photobleaching step (which constitutes "step e)" of the instant claim) are encompassed by the open claim language "comprising."

While Kawashima et al teach the labels are fluorescent labels (page 7, lines 15-22), and that the labels are removed (page 6, lines 25-26), Kawashima et al do not explicitly teach a cleavable link between the label and the nucleotide (i.e., claim 1) that is a disulfide (i.e., claim 10) and the linker is shorter than 8 atoms (i.e., claim 13). Thus, Kawashima et al teach a method that differs from the instantly claimed method because Kawashima et al do not teach a cleavable link between the label and the nucleotide.

However, Urdea et al teach detectably labeled nucleotides (column 8, lines 20-60), wherein the detectable label is a fluorescent label (column 4, lines 5-10) and is linked to the nucleotide with a cleavable linker in the form of a disulfide linker (i.e., claim 10; column 8, lines 20-60). The linker between the disulfide bridge and the base is less than 8 atoms; namely, Formula 13 has label R1, a disulfide for R2, x is one CH2 linker, and NH connects to the base (i.e., claim 13; column 8, lines 20-60). Urdea et al further teach that the nucleotides having the linkers and labels have the added advantage of being inexpensively synthesized in large quantity (column 2, lines 15-40). Thus, Urdea et al teach the known technique of using a cleavable link between a label and a nucleotide.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising the use of labeled nucleotides as taught by Kawashima et al with the labeled nucleotides having a disulfide linker (i.e., claims 1 and 10) that is less than 8 atoms (i.e., claim 13) as taught by Urdea et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of having a decreased cost as a result of being inexpensively synthesized in large quantity as explicitly taught by Urdea et al (column 2, lines 15-40). In addition, it would have been obvious to the ordinary artisan that the known technique of using the cleavable link of Urdea et al could have been applied to the method of Kawashima et al with

predictable results because the Urdea et al predictably results in a link useful in the labeling of nucleotides.

Regarding claims 2-3, method of claim 1 is discussed above. Kawashima et al also teach the amount of labeled derivative of the at least one nucleotide is within the range of 10-50 mole %; i.e., less than 50% (page 16, lines 15-23).

Regarding claim 4, method of claim 1 is discussed above. Kawashima et al also teach the single stranded nucleic acid is attached to a carrier; namely, immobilized to a surface of a bead (page 9, lines 20-25).

Regarding claim 5, method of claim 4 is discussed above. Kawashima et al also teach the means for attachment is specific binding to biotin/streptavidin (page 9, lines 10-15).

Regarding claim 6, method of claim 4 is discussed above. Kawashima et al also teach the carrier is a bead (page 9, lines 20-25).

Regarding claim 8, method of claim 1 is discussed above. Kawashima et al also teach the label is neutralized by photobleaching; namely, laser bleaching of the fluorophores, which are labels (page 18, lines 13-19).

Regarding claim 9, method of claim 1 is discussed above. Kawashima et al also teach the link between the incorporated nucleotide and the label is cleaved; namely, labels are removed periodically (i.e., cleaved; page 6, lines 25-26 and page 18, lines 14-20).

Regarding claim 16 method of claim 1 is discussed above. Kawashima et al also teach the agent Tween 20 is added (page 41, lines 5-11).

11. Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawashima et al (PCT International Application No. WO 98/44152, published 8 October 1998) in view of Urdea et al (U.S. Patent No. 4,910,300, issued 20 March 1990) as applied to claims 1 and 10 above, and further in view of Verdine (U.S. Patent No. 5,783,384, issued 21 July 1998).

Regarding claim 11, the method of claims 1 and 10 is discussed above in Section 10. Neither Kawashima et al nor Urdea teach cleavage is performed by addition of a reducing agent to expose and provide a thiol group.

However, Verdine teaches the attachment of molecules (i.e., peptides) to nucleotides using disulfide links, wherein the disulfide is cleaved to expose and provide a thiol by the addition of a reducing agent, which has the added advantage of allowing the determination of binding affinity of test molecules to the sequence (column 7, line 59-column 8, line 10). Thus, Verdine teach the known technique of rejecting a disulfide to from and provide an exposed thiol group.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising the use of disulfide linked labeled nucleotides as taught by Kawashima et al in view of Urdea et al with the reductive cleavage of the link to generate a thiol as taught by Verdine with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of allowing the determination of binding affinity of test molecules to the sequence as explicitly taught by Verdine (column 7; line 59-column 8, line 10). In addition, it would have been obvious to the ordinary artisan that the known technique of forming and providing an exposed thiol group of Verdine could have been applied to the method of Kawashima et al in view of Urdea with predictable results because the technique of forming and providing an exposed thiol group of Verdine predictably results in cleavage of the link.

Regarding claim 12, the method of claim 10 is discussed above on pages 6-8. Kawashima et al do not teach the exposed thiol is capped with iodoacetamide.

However, Verdine et al teach the capping (i.e., alkylation) of exposed thiols with iodoacetamide, which has the added advantage of allowing monitoring of the production of the thiols (column 10, lines 25-32), thereby verifying that the reduction of the disulfide to a thiol has worked. Thus, Verdine teaches the known technique of capping exposed thiols.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising the use of disulfide linked labeled nucleotides as taught by Kawashima et al in view of Urdea et al with the capping with iodoacetamide as taught by Verdine with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of allowing verification of the reductive production of free thiols by allowing monitoring of the production of the thiols as explicitly taught by Verdine (column 10, lines 25-32). In addition, it would have been obvious to the ordinary artisan that the known technique capping an exposed thiol group of Verdine could have been applied to the method of Kawashima et al in view of Urdea with predictable results because the technique of capping an exposed thiol group of Verdine predictably results in verification of the reduction reaction.

12. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawashima et al (PCT International Application No. WO 98/44152, published 8 October 1998) in view of Urdea et al (U.S. Patent No. 4,910,300, issued 20 March 1990) as applied to claim 1 above, and further in view of Uemori et al (PCT International Application Publication No. WO 97/24444, published 10 July 1997). Citations from Uemori et al are from the National Stage (U.S. Patent No. 6,395,526 B1, issued 28 May 2002). The National Stage is deemed an English language translation of the PCT.

Regarding claim 14, the method of claim 1 is discussed above in Section 10.

Neither Kawashima et al nor Urdea et al teach the extension with polymerase occurs at a pH below 7.

However, Uemori et al teach extension reactions of primer template/complexes using a DNA polymerase (Abstract) wherein the polymerase exhibits maximum activity at a pH of 6.5 (column 12, lines 13-16). Uemori et al also teach the DNA polymerase having the activity at pH 6.5 has the added advantage of higher primer extensibility (Abstract) with a lower error rate in DNA synthesis (column 13,

lines 30-35), which improves the assay accuracy. Thus, Uemori et al teach the known technique of performing primer extension at a pH below 7.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising the use of a DNA polymerase as taught by Kawashima et al in view of Urdea et al with the DNA polymerase of Uemori et al with a reasonable expectation of success. Use of the polymerase of Uemori et al would result in extension reactions performed at a pH 6.5. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method wherein the polymerase reactions are performed at a pH of 6.5 for maximum activity of a polymerase that has the added advantage of higher primer extensibility with improved assay accuracy as a result of the lower error rate in DNA synthesis of the polymerase as explicitly taught by Uemori et al (Abstract and column 13, lines 30-35). In addition, it would have been obvious to the ordinary artisan that the pH of Uemori et al could have been applied to the method of Kawashima et al in view of Urdea with predictable results because the pH of Uemori et al predictably results in a viable primer extension reaction.

13. Claims 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawashima et al (PCT International Application No. WO 98/44152, published 8 October 1998) in view of Urdea et al (U.S. Patent No. 4,910,300, issued 20 March 1990) as applied to claim 1 above, and further in view of Lee et al (Nucleic Acids Res., vol. 20, pages 2471-2483 (1992)).

Regarding claim 15, the method of claim 1 is discussed above in Section 10. Neither Kawashima et al nor Urdea et al teach dideoxynucleotides.

However, Lee et al teach a method of primer extension (i.e., incorporation) using fluorescently labeled dideoxynucleotides (Abstract), wherein the use dideoxy nucleotides in sequencing (i.e., determining the type of nucleotide added to a primer) has the added advantage of being the most

durable and efficient method of DNA sequence and is the method of choice in large scale sequencing programs (Introduction). Thus, Lee et al teach the known technique of using dideoxy nucleotides.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of by Kawashima et al in view of Urdea et al with the dideoxynucleotides of Lee et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of being the most durable and efficient method of DNA sequence and is the method of choice in large scale sequencing programs as explicitly taught by Lee et al (Introduction). In addition, it would have been obvious to the ordinary artisan that the labeled dideoxy nucleotides of Lee et al could have been applied to the method of Kawashima et al in view of Urdea with predictable results because the labeled dideoxy nucleotides of Lee et al predictably results nucleotides viable in a primer extension reaction.

Response to Arguments

14. Applicant's arguments filed 9 October 2007 (i.e., the "Remarks") have been fully considered but they are not persuasive for the reason(s) listed below.

A. Applicant argues on page 10 of the Remarks that Kawashima failed to specify that the label is neutralized after step d). Applicant cites page 6, lines 18-27 of Kawashima et al is support of the argument.

However, Applicant's citation explicitly teaches that "in some embodiments it may be desired to remove labels periodically." While Kawashima et al state there is no need to do so, Kawashima et al clearly teach embodiments wherein the labels are removed (see also page 18, lines 14-20). Thus, Kawashima et al do in fact teach neutralization (e.g., removal, photobleaching) of the label after determination of the type of nucleotide as detailed in the rejection above.

Applicant further argues on page 10 of the remarks that if labels are removed, they are only removed periodically, not after each detection step.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., removal after each detection step) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claim specifically recites "repeating steps c) to d) at least once," but does not necessarily require cleavage after every detection step because other steps similar to steps c) and d) can be performed between the completion of step d) but before step e). For example, as noted above in the rejection presented in Section 10, the open claim language "comprising" in line 2 of claim 1 encompasses additional steps between step d) and the "repeating steps c) to d) at least once" at the end of the claim. Thus, after a label is removed by photobleaching (i.e., step "d)" of the instant claims), multiple rounds of enzymatic extension with a mixture of labeled and unlabeled nucleotides and determination of the type of nucleotide added before a subsequent photobleaching step (which constitutes "step e)" of the instant claim) are encompassed by the open claim language "comprising."

B. Applicant argues on page 11 of the Remarks that Kawashima et al teaches away from the instant claims.

However, as noted above, Kawashima et al clearly teach embodiments wherein the labels are removed (see also page 18, lines 14-20). Thus, Kawashima et al do in fact teach neutralization (e.g., removal, photobleaching) of the label after determination of the type of nucleotide as detailed in the rejection above.

C. Applicant further argues on page 11 of the Remarks that pages 2-3 of the specification illustrate that Kawashima et al teach "no attempt to remove the signal incorporated."

However, as noted above, Kawashima et al clearly teach embodiments wherein the labels are removed (see also page 18, lines 14-20). Thus, Kawashima et al do in fact teach neutralization (e.g.,

removal, photobleaching) of the label after determination of the type of nucleotide as detailed in the rejection above.

D. Applicant argues on page 11 of the Remarks that in view of Kawashima et al and Urdea et al, the skilled artisan would not have a reason or expectation to remove a label after every detection step so that sensitive sequencing of longer sequences would be possible.,

In response to applicant's argument that the references fail to show certain features of applicant's invention, as noted above, the features upon which applicant relies (i.e., removal after each detection step) are not recited in the rejected claim(s). The claim specifically recites "repeating steps c) to d) at least once," but does not necessarily require cleavage after every detection step because other steps similar to steps c) and d) can be performed between the completion of step d) but before step e). For example, as noted above in the rejection presented in Section 10, the open claim language "comprising" in line 2 of claim 1 encompasses additional steps between step d) and the "repeating steps c) to d) at least once" at the end of the claim. Thus, after a label is removed by photobleaching (i.e., step "d)" of the instant claims), multiple rounds of enzymatic extension with a mixture of labeled and unlabeled nucleotides and determination of the type of nucleotide added before a subsequent photobleaching step (which constitutes "step e)" of the instant claim) are encompassed by the open claim language "comprising."

In addition, the claim does not recite any limitations regarding the length (i.e., of longer) sequences. Thus, the features upon which applicant relies are not recited in the rejected claim(s).

Furthermore, Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

Applicant also argues on page 12 of the Remarks that neither publication provides a reason for combining and modifying the publications to obtain step d of the method of claim 1.

However, as noted in the above, Kawashima et al teach the limitations of step d) as claimed. Urdea is solely relied upon for a cleavable linker in the form of a disulfide linker (i.e., claims 1 and 10), wherein the linker between the disulfide bridge and the base is less than 8 atoms (i.e., claim 13).

In addition, it is also noted that under the Supreme Court ruling for *KSR Int'l Co. v. Teleflex, Inc* (No 04-1350 (US 30 April 2007) forecloses the argument that a specific teaching suggestion, or motivation is required to support a finding of obviousness. See *Ex parte Smith* (USPQ2d, slip op. at 20 (Bd. Pat. App. & Interf. June 25, 2007).

E. The remaining arguments regarding the dependent claims rely on arguments set forth to address the rejections of independent claim 1 under 35 USC 103(a). These arguments are addressed above. Since the arguments regarding independent claim 1 were not persuasive, the rejections of the dependent claims are maintained.

Conclusion

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

17. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing

date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jehanne Sitton/
Primary Examiner
12/5/2007

Robert T. Crow
Examiner
Art Unit 1634